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FILE 'CAPLUS' ENTERED AT 16:10:20 ON 28 APR 2005

=> ACTIVATE ABZYME/Q
L1              QUE  ABB=ON  PLU=ON  ((CATALYSIS OR CATALYZES OR CATALYTIC OR C
                ATALYZED)(5A)ANTIBOD?) OR ABZYME

=> S L1
         175719 CATALYSIS
            419 CATALYSES
         175958 CATALYSIS
                  (CATALYSIS OR CATALYSES)
          33622 CATALYZES
         383617 CATALYTIC
             27 CATALYTICS
         383627 CATALYTIC
                  (CATALYTIC OR CATALYTICS)
         223017 CATALYZED
              1 CATALYZEDS
         223017 CATALYZED
                  (CATALYZED OR CATALYZEDS)
         431324 ANTIBOD?
           2269 (CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
            248 ABZYME
            155 ABZYMES
            295 ABZYME
                  (ABZYME OR ABZYMES)
L2         2295 ((CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?)
                 OR ABZYME

=> S TNF(W)ALPHA
          54119 TNF
            111 TNFS
          54126 TNF
                  (TNF OR TNFS)
        1537362 ALPHA
           2479 ALPHAS
        1537462 ALPHA
                  (ALPHA OR ALPHAS)
L3        39604 TNF(W)ALPHA

=> S IL(W)6;S VEGFR2
         103113 IL
            853 ILS
         103744 IL
                  (IL OR ILS)
        3551908 6
L4        23718 IL(W)6


L5          378 VEGFR2

=> S PHAGE DISPLAY;S IN VIVO SCREENING;S HIGH THROUGHPUT SCREENING;S BETA(W)LACTAM;S
CEFOXITIN;S CEFOTAXIME
          45452 PHAGE
           7383 PHAGES
          47091 PHAGE
                  (PHAGE OR PHAGES)
         163395 DISPLAY
          71651 DISPLAYS
         203381 DISPLAY
                  (DISPLAY OR DISPLAYS)
L6         4631 PHAGE DISPLAY
                  (PHAGE(W)DISPLAY)
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         395464 VIVO
              1 VIVOS
         395464 VIVO
                  (VIVO OR VIVOS)
         165053 SCREENING
           1548 SCREENINGS
         166235 SCREENING
                  (SCREENING OR SCREENINGS)
L7          347 IN VIVO SCREENING
                  (VIVO(W)SCREENING)


        3552202 HIGH
            545 HIGHS
        3552507 HIGH
                  (HIGH OR HIGHS)
          34231 THROUGHPUT
           1147 THROUGHPUTS
          35144 THROUGHPUT
                  (THROUGHPUT OR THROUGHPUTS)
         165053 SCREENING
           1548 SCREENINGS
         166235 SCREENING
                  (SCREENING OR SCREENINGS)
L8         7803 HIGH THROUGHPUT SCREENING
                  (HIGH(W)THROUGHPUT(W)SCREENING)


        1312109 BETA
           1323 BETAS
        1312180 BETA
                  (BETA OR BETAS)
          27041 LACTAM
          18021 LACTAMS
          34260 LACTAM
                  (LACTAM OR LACTAMS)
L9        16608 BETA(W)LACTAM


L10        3151 CEFOXITIN


           5660 CEFOTAXIME
              1 CEFOTAXIMES
L11        5660 CEFOTAXIME
                  (CEFOTAXIME OR CEFOTAXIMES)

=> S L1 AND (L3,L4,L5)
         175719 CATALYSIS
            419 CATALYSES
         175958 CATALYSIS
                  (CATALYSIS OR CATALYSES)
          33622 CATALYZES
         383617 CATALYTIC
             27 CATALYTICS
         383627 CATALYTIC
                  (CATALYTIC OR CATALYTICS)
         223017 CATALYZED
              1 CATALYZEDS
         223017 CATALYZED
                  (CATALYZED OR CATALYZEDS)
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        431324 ANTIBOD?
          2269 (CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
           248 ABZYME
           155 ABZYMES
           295 ABZYME
                 (ABZYME OR ABZYMES)
L12          1 L1 AND ((L3 OR L4 OR L5))

=> D CBIB ABS

L12  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
2005:303304  Adzymes comprising fusions of enzyme catalytic moieties
     and receptor or antibody targeting moieties and their use for
     treatment of target-associated diseases.  Afeyan, Noubar B.; Lee, Frank
     D.; Wong, Gordon G.; Das Gupta, Ruchira; Baynes, Brian (Compound
     Therapeutics, Inc., USA).  U.S. Pat. Appl. Publ. US 20050074865 A1
     20050407, 123 pp., Cont.-in-part of U.S. Ser. No. 650,592.  (English).
     CODEN: USXXCO.  APPLICATION: US 2004-792498 20040302.  PRIORITY: US
     2002-PV406517 20020827; US 2002-PV423754 20021105; US 2002-PV430001
     20021127; US 2003-650592 20030827.
AB   Disclosed is a family of novel protein constructs, useful as drugs and for other
     purposes, termed "adzymes," comprising an address moiety and a catalytic domain.
     In some types of disclosed adzymes, the address binds with a binding site on or
     in functional proximity to a targeted biomol., e.g., an extracellular targeted
     biomol., and is disposed adjacent the catalytic domain so that its affinity
     serves to confer a new specificity to the catalytic domain by increasing the
     effective local concentration of the target in the vicinity of the catalytic
     domain.  The invention is partially based on the unexpected discovery that, when
     designing adzymes, certain kinetic properties of the final adzyme can be altered
     to achieve a balance between optimal selectivity and optimal adzyme potency.  As
     the enzyme or catalytic domain of an adzyme becomes more potent, the overall
     adzyme quickly loses its selectivity against a panel of different substrates,
     thus compromising the overall usefulness of the enzyme.  On the other hand, if
     maximal selectivity is to be achieved without regard to potency, the potency can
     quickly approach that of a stoichiometric binder, e.g., the address domain or
     targeting moiety, and again compromise the overall usefulness of the adzyme.  The
     optimal balance is achieved when the catalytic efficiency of the enzyme domain
     (kcatES/KmES) is equal to koffAS/[S]eff, which can be most efficiently achieved
     by adjusting [S]eff, such as by adjusting the length of the linker between the
     catalytic domain and the targeting moiety.  The invention is exemplified by
     construction of adzymes targeting tumor necrosis factor-α and comprising
     trypsin(ogen) or mesotrypsin(ogen) fused to tumor necrosis factor receptor I p55
     subunit or an anti-(TNFα) scFv antibody. The present invention also provides
     pharmaceutical compns. comprising these adzymes, methods of making adzymes, DNAs
     encoding adzymes or parts thereof, and methods of using adzymes, such as for
     treating human subjects suffering from a disease, such as a disease associated
     with a soluble or membrane bound mol., e.g., an allergic or inflammatory disease.


=> S L1 AND (L6,L7,L8)
        175719 CATALYSIS
           419 CATALYSES
        175958 CATALYSIS
                 (CATALYSIS OR CATALYSES)
         33622 CATALYZES
        383617 CATALYTIC
            27 CATALYTICS
        383627 CATALYTIC
                 (CATALYTIC OR CATALYTICS)
        223017 CATALYZED
             1 CATALYZEDS
        223017 CATALYZED
                 (CATALYZED OR CATALYZEDS)
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        431324 ANTIBOD?
          2269 (CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
           248 ABZYME
           155 ABZYMES
           295 ABZYME
                (ABZYME OR ABZYMES)
L13         68 L1 AND ((L6 OR L7 OR L8))

=> D 1-68 TI
=> D 1,3,8,10,13,14,16,18,20-22,25,28-30,41,48,50,55,56,58,62,63,65 CBIB ABS

L13  ANSWER 1 OF 68  CAPLUS  COPYRIGHT 2005 ACS on STN
2005:149232  Spectrophotometric enzyme assays for high-
     throughput screening.  Reymond, Jean-Louis (Department
     of Chemistry and Biochemistry, University of Bern, Bern, CH-3012, Switz.).
     Food Technology and Biotechnology, 42(4), 265-269 (English) 2004.  CODEN:
     FTBRFD.  ISSN: 1330-9862.  Publisher: University of Zagreb, Faculty of
     Food Technology and Biotechnology.
AB   This paper reviews high-throughput screening enzyme assays developed in our
     laboratory over the last ten years.  These enzyme assays were initially developed
     for the purpose of discovering catalytic antibodies by screening cell culture
     supernatants, but have proved generally useful for testing enzyme activities.
     Examples include TLC-based screening using acridone-labeled substrates,
     fluorogenic assays based on the β-elimination of umbelliferone or nitrophenol,
     and indirect assays such as the back-titration method with adrenaline and the
     copper-calcein fluorescence assay for amino acids.


L13  ANSWER 3 OF 68  CAPLUS  COPYRIGHT 2005 ACS on STN
2004:1074809  Directed evolution governed by controlling the molecular
     recognition between an abzyme and its haptenic transition-state
     analog.  Takahashi-Ando, Naoko; Kakinuma, Hiroyuki; Fujii, Ikuo; Nishi,
     Yoshisuke (Laboratory of Life Science and Biomolecular Engineering, Japan
     Tobacco, Inc., Aoba-ku, Yokohama, Kanagawa, 227-8512, Japan).  Journal of
     Immunological Methods, 294(1-2), 1-14 (English) 2004.  CODEN: JIMMBG.
     ISSN: 0022-1759.  Publisher: Elsevier B.V..
AB   The catalytic antibody, 6D9, was subjected to directed evolution in the phage-
     display system using two structurally related transition-state analogs (TSAs) for
     panning.  One analog, TSA 3, was originally used for immunization, and the other,
     TSA 4, a derivative of TSA 3, was designed to optimize the differential affinity
     for the transition state relative to the ground state so as to provide variants
     with improved reaction rates.  We previously reported that by panning with TSA 4,
     we could obtain variants with highly improved catalytic rate enhancement
     (kcat/kuncat), and Tyr (L27e) seemed to play a key role in stabilizing the
     transition-state structure [Nat. Biotechnol. 19 (2001) 563].  Here, we examined
     in detail a large number of the variants selected by these haptens, in order to
     elucidate the mechanism of the directed evolution driven by them.  ELISA with 3-
     and 4-bovine serum albumin (BSA) showed that variants selected by these TSAs
     exhibited distinct binding patterns.  All the variants whose rate enhancement was
     greater than five-fold of that of 6D9 had Tyr (L27e) and were obtained from the
     library panned with TSA 4, but not from the library panned with TSA 3.  Kinetic
     studies showed that TSA 4 could efficiently select variants with increased
     differential binding affinity for the transition state relative to the ground
     state, and these variants exhibited improved rate enhancements.  This study
     verified the difference of in vitro evolution driven by the two structurally
     related TSAs and stresses the importance of designing an appropriate hapten for
     panning.


L13  ANSWER 8 OF 68  CAPLUS  COPYRIGHT 2005 ACS on STN
2004:44842  Document No. 141:186808  Mechanistic studies of an oxy-Cope
     catalytic antibody and high throughput
     screening of enzyme function.  Varvak, Alexander (Univ. of
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California, Berkeley, CA, USA). 122 pp. Avail. UMI, Order No. DA3082444 From: Diss. Abstr. Int., B 2003, 64(2), 723 (English) 2002.

AB Unavailable

L13 ANSWER 10 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

2004:4105 Document No. 140:124537 Development of a high-throughput screen for protein catalysts: Application to the directed evolution of antibody aldolases. Gildersleeve, Jeff; Varvak, Alex; Atwell, Shane; Evans, Doug; Schultz, Peter G. (Department of Chemistry, The Scripps Research Institute, La Jolla, CA, 92037, USA). Angewandte Chemie, International Edition, 42(48), 5971-5973 (English) 2003. CODEN: ACIEF5. ISSN: 1433-7851. Publisher: Wiley-VCH Verlag GmbH & Co. KGaA.

AB A semiautomated high-throughput system has been developed to express and purify proteins and assay their catalytic activity. The screen can be used to evolve activity, selectivity, and expression levels of proteins directly or in combination with selections. To illustrate its potential, the system was applied to the directed evolution of catalytic antibodies with aldolase activity.

L13 ANSWER 13 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

2003:668267 Document No. 140:177098 Phage display as a tool for the directed evolution of enzymes. Fernandez-Gacio, Ana; Uguen, Marilyne; Fastrez, Jacques (Institut des Sciences de la Vie, Laboratoire de Biochimie Physique et des Biopolymeres, Universite Catholique de Louvain, Louvain-la-Neuve, B1348, Belg.). Trends in Biotechnology, 21(9), 408-414 (English) 2003. CODEN: TRBIDM. ISSN: 0167-7799. Publisher: Elsevier Science Ltd..

AB A review. Since its introduction in 1985, phage display has had a tremendous impact on the discovery of peptides that bind to a variety of receptors, the generation of binding sites within predefined scaffolds, and the creation of high-affinity antibodies without immunization. Its application to enzymol. has required the development of techniques that couple enzymic activity to selection protocols based on affinity chromatog. Here, we describe both indirect methods, using transition-state analogs and suicide substrates, and direct methods, using the ability of active phage-enzymes to transform substrate into product. The methods have been applied to large libraries for mechanistic-based studies and to generate variants with new or improved properties. In addition, such techniques have been successfully used to select catalytic antibodies and improve their catalytic efficiency.

L13 ANSWER 14 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

2003:645519 Document No. 139:302529 Development of a novel display system for screening in production of catalytic antibodies. Ueda, Mitsuyoshi; Lin, Ying; Kondo, Akihiko; Fujii, Ikuo (Graduate School of Engineering, Kyoto University, Japan). Bio Industry, 20(7), 15-22 (Japanese) 2003. CODEN: BIINEG. ISSN: 0910-6545. Publisher: Shi Emu Shi Shuppan.

AB A review. Advantage of the use of catalytic antibodies in synthesis of novel substances was first discussed with an example of derivatization by the catalytic antibody 6D9 of chloramphenicol. The impact of cell surface engineering in display screening and the application to displaying catalytic antibodies were described. The visualization of the screening and binding kinetics anal. by the use fluorescence indicators such as FITC was also discussed.

L13 ANSWER 16 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

2003:319446 Document No. 138:336413 Covalently reactive transition state analogs (CRTSA) of antibody for treating autoimmune, microbial, lymphoproliferative and neoplastic diseases and for screening phage display library and B cell-expressing surface antibody. Paul, Sudhir; Nishiyama, Yasuhiro (Board of Regents, The

University of Texas System, USA). U.S. Pat. Appl. Publ. US 2003078203 A1 20030424, 52 pp., Cont.-in-part of U.S. Ser. No. 862,849. (English). CODEN: USXXCO. APPLICATION: US 2002-114716 20020401. PRIORITY: US 1998-46373 19980323; US 2001-PV280624 20010331; US 2001-862849 20010522.

AB The CRTSA of antibodies or catalytic antibodies comprise an epitope of a target protein antigen, an electrophilic covalently reactive center bearing a partial or full neg. charge and an electron withdrawing (or donating) substituent optionally containing a flanking peptide sequence. The provided CRTSA are useful for production, selection and inhibition of catalytic antibodies specific to tumor necrosis factor, epidermal growth factor receptor, interleukin 1, gp120, gp160, gag, pol, HBsAg, bacterial exotoxin, EGF, TGFα, p53, prostate-specific antigen, CEA, prolactin, hCG, c-myc, c-fos, c-jun, HER-2, prolactin receptor, steroid receptor and interleukin 4. The CRTSA antibodies are therefore useful as vaccine or for passive immunotherapy of autoimmune diseases, lymphoproliferative diseases, microbial infection,. The CRTSA antibodies are also useful for screening phage displaying or B cell expressing catalytic antibodies on the surface.

L13 ANSWER 18 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

2003:184751 In vivo and in vitro evolution of catalytic antibodies. Yin, Jun; Beuscher, Albert E.; Andryski, Scott; Stevens, Raymond C.; Schultz, Peter G. (Department of Chemistry, The Scripps Research Institute, La Jolla, CA, 92037, USA). Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003, ORGN-257. American Chemical Society: Washington, D. C. (English) 2003. CODEN: 69DSA4.

AB Antibody 7G12 was raised against N-methylmesoporphyrin (NMP) and catalyzes porphyrin metalation with catalytic efficiency approaching that of the enzyme ferrochelatase. The X-ray crystal structure of 7G12 Fab-mesoporphyrin (MP) complex shows the antibody bound porphyrin substrate is distorted from the planar conformation and provides unequivocal evidence for the strain theory of enzyme catalysis proposed by Haldane in the 1930s. A comparison of the crystal structures of the germline and affinity-matured 7G12 antibodies reveals that the germline antibody undergoes significant conformational changes upon the binding of either hapten NMP or non-hapten ligand jeffamine and during affinity maturation, somatic mutations preorganize the affinity-matured antibody for specific hapten binding and porphyrin distortion. This may be a general strategy not only for immunol. evolution of antibodies, but for natural evolution of biol. catalysts as well. We have also developed a phage display system for in vitro evolution of the peroxidase activity of antibody 7G12-heme complex.

L13 ANSWER 20 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

2002:787392 Document No. 138:51780 A method for the detection and screening of catalytic anti-DNA antibodies. Mouratou, Barbara; Rouyre, Sylvie; Guesdon, Jean-Luc (Laboratoire d'Ingenierie des Anticorps, Institut Pasteur, Paris, 75724, Fr.). Journal of Immunological Methods, 269(1-2), 147-155 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..

AB We have developed a microtiter plate assay for the detection and screening of anti-DNA hydrolytic antibodies. The affinity-linked oligonucleotide nuclease assay (ALONA) makes use of substrates with a digoxigenin on the 5'-end of the 3'-biotinylated DNA strands. The substrate binds specifically to the wells of streptavidin-coated microtiter plates where the reaction takes place. Uncleaved substrate retains the digoxigenin label, which is then detected with an enzyme-labeled anti-digoxigenin antibody. We first assessed the efficiency of this assay by measuring S1 nuclease and DNase I activities and the inhibitory effect of EDTA on the reaction. The ALONA procedure was then successfully applied to the screening of a high number of hybridoma clones derived from nonimmunized (NZB+NZW)F1 mice with spontaneous lupus erythematosus. We detected three potential catalytic antibodies and investigated their substrate specificity. Overall, our findings demonstrate the value of the ALONA method for high

throughput screening of potential nucleases and catalytic antibodies. Although this assay was designed for the selection of catalysts active in DNA hydrolysis, it can be adapted to detect most types of substrate cleavage reaction.

L13 ANSWER 21 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
2002:787388 Document No. 138:52234 Detection strategies for catalytic antibodies. Reymond, Jean-Louis (Departement fur Chemie und Biochemie, Universitat Bern, Bern, 3012, Switz.). Journal of Immunological Methods, 269(1-2), 125-131 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..

AB This paper discusses the detection of antibody catalysis using soluble test substrates. Antibodies raised against a transition state analog of a chemical reaction typically show dissociation consts. for the antibody-hapten complexes in the range of 10-9-10-7 M. If hapten binding is transferred to catalysis as measured by the transition-state dissociation constant KTS=KM/(kcat/kuncat)=kuncat/(kcat/KM), this corresponds to the concentration of antibody necessary to double the apparent rate of the reaction. This sets a lower limit for the detection of catalysis if no addnl. effects are present to induce catalysis. The concentration of antibodies in hybridoma cell culture supernatants (5-50 μg/mL) meets this requirement. The use of high-throughput screening (HTS) for catalysis together with ELISA to select hybridomas leads to the isolation of not only one, but also many catalytic antibodies. As examples, the application of HTS for catalysis using fluorogenic reactions to isolate retro-Diels-Alderase and pivalase catalytic antibodies useful for prodrug activation chemical are discussed.

L13 ANSWER 22 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
2002:777955 Document No. 137:290932 Covalently reactive transition state analogs for use in therapeutic inhibition or production of catalytic antibodies. Paul, Sudhir; Nishiyama, Yasuhiro (Board of Regents, the University of Texas System, USA). PCT Int. Appl. WO 2002079223 A2 20021010, 87 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US10116 20020401. PRIORITY: US 2001-PV280624 20010331.

AB Covalently reactive transition state analogs (CRTSAs) R1-E-R2 (R1 = peptide epitope of target antigen; E = electrophilic, covalently reactive, charged center; R2 = electron donating or withdrawing group optionally attached to another peptide) and their use in inhibiting disease-related catalytic antibodies or in stimulating production of catalytic antibodies with desirable activities are disclosed. The CRTSAs may also be used to select phage display catalytic antibodies or to select B cells displaying catalytic antibodies on their surface. Thus, N-acyl derivs. of amino(4-amidinophenyl)methanephosphonate esters were prepared These phosphonates irreversibly inhibited trypsin, thrombin, and catalytic antibodies. Other phosphonates were used to isolate catalytically active subtilisin mutants or proteolytically active Fv and L chains from phage libraries.

L13 ANSWER 25 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
2002:476860 Document No. 137:43274 Development of phage display. High activation of catalytic antibodies . Fujii, Ikuo (Biomol. Eng. Res. Inst., Japan). Kagaku to Seibutsu, 40(6), 396-401 (Japanese) 2002. CODEN: KASEAA. ISSN: 0453-073X. Publisher: Gakkai Shuppan Senta.

AB A review on functional modification of antibody proteins using phage display, focusing on high activation of catalytic antibodies. Topics discussed include preparation of catalytic antibodies, specific activation of prodrugs by catalytic antibody, and high activation of catalytic antibodies using antibody phage display libraries.

L13 ANSWER 28 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
2002:332361 Document No. 136:321704 Methods and compositions for modifying biologically active target molecules with catalytic antibodies. Martin, Mark T. (Igen International, Inc., USA). PCT Int. Appl. WO 2002034933 A2 20020502, 61 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US31663 20011010. PRIORITY: US 2000-PV242125 20001020.

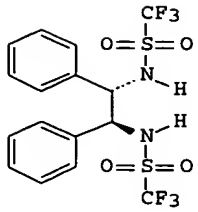
AB The invention concerns a method of modifying a target substance by contacting the target substance with a catalyst that catalyzes the modification of the target substance. In a preferred embodiment, the method comprises labeling a target substance by contacting the target substance with a label and a catalyst that catalyzes the attachment of the label to the target substance. Preferably, the catalyst catalyzes selectively the reaction between a specific target mol. and a specific label. The attachment of labels may be used to inactivate a biol. active target substance or otherwise modulate its activity. Alternatively, the method may be used to label the target mol. with a detectable label suitable for the sensitive detection of the target substance.

L13 ANSWER 29 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
2002:110728 Document No. 136:212930 New high-throughput screening assays for biocatalysis. Reymond, Jean-Louis (Department of Chemistry and Biochemistry, University of Bern, Bern, CH-3012, Switz.). Chimia, 55(12), 1049-1052 (English) 2001. CODEN: CHIMAD. ISSN: 0009-4293. Publisher: Neue Schweizerische Chemische Gesellschaft.

AB A review. High-throughput screening for catalysis is a critical technol. in all expts. aimed at modifying or creating enzymes by directed evolution, as well as for biodiversity mining for new catalysts. We have developed a series of enzyme assays based on fluorogenic substrates and on fluorescent product sensors. These new assays offer the possibility to assay chemical non-activated functional groups within chiral mols. with unprecedented sensibility and selectivity. Assays are exemplified for alc. dehydrogenases, aldolases, lipases and esterases, amidases and acylases, phosphatases, and epoxide hydrolases. The assays can also be used to isolate catalytic antibodies by screening libraries produced by immunization with transition-state analogs. These assays are suitable for microtiter plate and higher miniaturization formats.

L13 ANSWER 30 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
2002:59239 Document No. 136:369474 Communications: High-throughput screening of enantioselective catalysts by immunoassay. Taran, Frederic; Gauchet, Cecile; Mohar, Barbara; Meunier, Stephane; Valleix, Alain; Renard, Pierre Yves; Creminon, Christophe; Grassi, Jacques; Wagner, Alain; Mioskowski, Charles (Laboratoire de Synthese Bioorganique (UMR 7514), Universite Louis Pasteur, Illkirch-Graffenstaden, 67401, Fr.). Angewandte Chemie, International Edition, 41(1), 124-127 (English) 2002. CODEN: ACIEF5. ISSN: 1433-7851. OTHER SOURCES: CASREACT 136:369474. Publisher: Wiley-VCH Verlag GmbH.

GI



I

AB Immunoassay techniques are demonstrated for anal. of catalytic activity of a combinatorial library of enantioselective reduction catalysts. By using an antibody that binds indiscriminately to the two enantiomers of the reduction product, the yield of the reaction can be calculated, and subsequently employing an enantiospecific antibody the enantiomeric excess can be determined This method was demonstrated on a combinatorial library of reduction catalyst prepared by combining a set of 22 chiral diamine-based ligands, e.g., I, with four different metal species. As a model reaction, the enantioselective reduction of benzoyl formic acid to (S)-mandelic acid was studied identifying the optimal catalyst as a combination of [RuCl2(p-cym)]2 with the chiral diamine ligand I.

L13 ANSWER 41 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
2001:110327 Document No. 134:322435 Specific Glycosidase Activity Isolated from a Random Phage Display Antibody Library. Goud, Gaddam Narsa; Artsaenko, Olga; Bols, Mikael; Sierks, Michael (Department of Chemical and Biochemical Engineering, University of Maryland Baltimore County, Baltimore, MD, 21250, USA). Biotechnology Progress, 17(1), 197-202 (English) 2001. CODEN: BIPRET. ISSN: 8756-7938. Publisher: American Chemical Society.

AB Carbohydrates serve as key receptor sites in various cellular events such as viral attachment, tumor formation, and tissue inflammation. A potential route to control these events is to manipulate targeted carbohydrate structures in vivo using specifically designed glycohydrolases. Here we show that a stereospecific catalytic activity designed toward a particular sugar and linkage can be readily isolated from a phage display antibody library derived from a nonimmunized host. The activity was isolated using a transition-state analog mimicking an α-glucosidasic linkage as antigen and showed a 20-fold specificity for that sugar and linkage. The DNA sequence, however, contains a large deletion in the antibody gene, which also changes the downstream reading frame, resulting in a translated sequence containing only 57 amino acids that has a predominantly hydrophobic amino terminal and a strongly hydrophilic carboxy terminal. The isolated catalytic activity has a strong pH dependence, attributable to one or more of the numerous potentially charged groups in the carboxyl terminal. While the protein readily forms more stable multimers, the 7.3 kDa monomer represents by far the smallest glycosidase enzyme reported to date and can provide substantial new information toward understanding and modifying glycosidase activity.

L13 ANSWER 48 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
1999:710046 Document No. 133:39705 Catalytic single-chain antibodies possessing β-lactamase activity selected from a phage displayed combinatorial library using a mechanism-based inhibitor. Tanaka, Fujie; Almer, Helena; Lerner, Richard A.; Barbas, Carlos F., III (The Skaggs Institute for Chemical Biology and the Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA). Tetrahedron Letters, 40(46), 8063-8066 (English) 1999. CODEN: TELEAY.

ISSN: 0040-4039. Publisher: Elsevier Science Ltd..

AB Catalytic single-chain antibodies (scFvs) possessing β-lactamase activity were selected from a phage displayed combinatorial antibody library using a penam sulfone mechanism-based inhibitor of β-lactamase. The scFvs FT6 and FT12 catalyzed the hydrolysis of ampicillin with rate accelerations (kcat/kuncat) of 5200 and 320.

L13 ANSWER 50 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

1999:372202 Document No. 131:55571 Directed evolution of antibody catalysts. Fujii, Ikuo (Biomol. Eng. Res. Inst., Japan). Seibutsu Butsuri, 39(3), 172-175 (Japanese) 1999. CODEN: SEBUAL. ISSN: 0582-4052. Publisher: Nippon Seibutsu Butsuri Gakkai.

AB A review with 11 refs. on mol. evolution of catalytic antibodies and their uses in studies of enzyme function mechanism and mol. evolution. Mechanism of production of antibody proteins is outlined, and mol. evolution of antibody is compared with that of enzymes. Two studies on antibody catalysts correlated with mol. evolution are introduced. One is "Reactive Immunization", a novel method for selection of antibody in immune system. The other is "phage antibody method". Principle of antibody phage display system is outlined, and recent studies on activity of antibody catalysts and improvement of substrate specificity (affinity maturation) are introduced.

L13 ANSWER 55 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

1998:790914 Document No. 130:34797 Recent advances of catalytic antibodies. Fujii, Ikuo; Tsumuraya, Takeshi (Biomol. Eng. Res. Inst., Suita, 565, Japan). Kagaku to Seibutsu, 36(12), 778-785 (Japanese) 1998. CODEN: KASEAA. ISSN: 0453-073X. Publisher: Gakkai Shuppan Senta.

AB A review with 18 refs. Techniques for preparation of catalytic antibodies by heterologous immunization, reactive immunization, and antibody phage display systems.

L13 ANSWER 56 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

1998:309067 Document No. 129:78488 Evolving catalytic antibodies in a phage-displayed combinatorial library. Fujii, Ikuo; Fukuyama, Shiro; Iwabuchi, Yoshiharu; Tanimura, Ryuji (Biomol. Eng. Res. Inst, Suita, Osaka, 565, Japan). Nature Biotechnology, 16(5), 463-467 (English) 1998. CODEN: NABIF9. ISSN: 1087-0156. Publisher: Nature America.

AB In vitro affinity maturation for evolving catalytic antibodies has been demonstrated by generating a diverse repertoire of the appropriate complementarity-determining regions on a phage surface. Phage display is followed by a selection based on binding to an altered antigen that was not used at the time of immunization, and provides variants with new catalytic activity and substrate specificity. This library format reduces the time needed to isolate the desired catalytic antibody fragments to under 2 wk.

L13 ANSWER 58 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

1997:624985 Document No. 127:304603 Phage display of a catalytic antibody to optimize affinity for transition-state analog binding. Baca, Manuel; Scanlan, Thomas S.; Stephenson, Robert C.; Wells, James A. (Department of Protein Engineering, Genentech, Inc., South San Francisco, CA, 94080, USA). Proceedings of the National Academy of Sciences of the United States of America, 94(19), 10063-10068 (English) 1997. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Catalytic antibodies have shown great promise for catalyzing a tremendously diverse set of natural and unnatural chemical transformations. However, few catalytic antibodies have efficiencies that approach those of natural enzymes. In principle, random mutagenesis procedures such as phage display could be used

to improve the catalytic activities of existing antibodies; however, these studies have been hampered by difficulties in the recombinant expression of antibodies. Here, we have grafted the antigen binding loops from a murine-derived catalytic antibody, 17E8, onto a human antibody framework in an effort to overcome difficulties associated with recombinant expression and phage display of this antibody. "Humanized" 17E8 retained similar catalytic and hapten binding properties as the murine antibody while levels of functional Fab displayed on phage were 200-fold higher than for a murine variable region/human constant region chimeric Fab. This construct was used to prepare combinatorial libraries. Affinity panning of these resulted in the selection of variants with 2-8-fold improvements in binding affinity for a phosphonate transition-state analog. Surprisingly, none of the affinity-matured variants was more catalytically active than the parent antibody and some were significantly less active. By contrast, a weaker binding variant was identified with 2-fold greater catalytic activity and incorporation of a single substitution (Tyr-100aH → Asn) from this variant into the parent antibody led to a 5-fold increase in catalytic efficiency. Thus, phage display methods can be readily used to optimize binding of catalytic antibodies to transition-state analogs, and when used in conjunction with limited screening for catalysis can identify variants with higher catalytic efficiencies.

L13 ANSWER 62 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

1996:391215 Document No. 125:80129 Selection of linkers for a catalytic single-chain antibody using phage display technology. Tang, Ying; Jiang, Ning; Parakh, Cushrow; Hilvert, Donald (Dep. Chem. Mol. Biol., Scripps Res. Inst., La Jolla, CA, 92037, USA). Journal of Biological Chemistry, 271(26), 15682-15686 (English) 1996. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Phage display has been evaluated as a means of rapidly selecting tailored linkers for single-chain antibodies (scFvs) from protein linker libraries. Preliminary expts. with a conventional linker failed to yield a functional single-chain version of a catalytic antibody with chorismate mutase activity. A random linker library was therefore constructed in which the genes for the heavy and light chain variable domains were linked by a segment encoding an 18-amino acid polypeptide of variable composition The scFv repertoire (≈5+106 different members) was displayed on filamentous phage and subjected to affinity selection with hapten. The population of selected variants exhibited significant increases in binding activity but retained considerable sequence diversity. Screening 1054 individual variants subsequently yielded a catalytically active scFv that was produced efficiently in soluble form. Sequence anal. revealed a conserved proline in the linker two residues after the VH C terminus and an abundance of arginines and prolines at other positions as the only common features of the selected tethers. There are apparently many viable solns. to the problem of linking individual VH and VL domains, but subtle differences in sequence dramatically influence the production, stability, and recognition properties of the scFv. The success of these expts. suggests that phage display will be generally useful for identifying peptide sequences for covalently linking any two protein domains.

L13 ANSWER 63 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

1995:988170 Document No. 124:23319 The isolation and production of catalytic antibodies using phage technology. Smith, Rodger G.; McCafferty, John; Chiswell, David; Darsley, Michael J.; Fitzgerald, Kevin; Kenten, John H.; Martin, Mark T.; Titmas, Richard C.; Williams, Richard O. (Igen, Inc., USA). PCT Int. Appl. WO 9527045 A1 19951012, 133 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1994-US3420 19940330.

AB Disclosed and claimed are methods for producing catalytic antibodies, including human catalytic antibodies , from bacteriophage. The methods require the cloning, selection, screening, and isolation of catalytic antibodies. Also disclosed and claimed are the catalytic antibodies made from the phage technol. In addition, catalytic antibodies produced from the phage technol. and useful in prodrug activation are disclosed and claimed. And finally, the invention also understands the production of catalytic antibodies to phosphonates. The RT3 hapten, 4-(carboxymethyl)phenyl- (2,4,6,trimethylphenyl)methyl phosphonate, was synthesized, conjugated to keyhole limpet hemocyanin, and the conjugate used to immunize mice. A plasmid allowing cloning of DNA encoding scFv fragments and phage display of scFv libraries was prepared The scFv coding regions are fused to a region encoding an His hexapeptide fused to a myc tag peptide. ScFv mols. which bind to the hapten were identified by panning and the sequences of some of these antibody fragments were determined The RT3-binding scFv's were screened for catalytic activity and several were found which were catalytically active at pH 7.0 and/or pH 9.0. RT3-binding scFv's were also prepared from a naive human antibody library and by chain or CDR shuffling.

L13 ANSWER 65 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
1995:817157 Document No. 123:253847 Selection of human immunoglobulin light chains from a phage-display library. Tyutyulkova, Sonia; Gao, Qing-Sheng; Paul, Sudhir (Medical Center, University Nebraska, Omaha, NE, USA). Methods in Molecular Biology (Totowa, New Jersey), 51(Antibody Engineering Protocols), 377-94 (English) 1995. CODEN: MMBIED. ISSN: 1064-3745. Publisher: Humana.
AB Asthma is associated with increased catalytic autoantibodies to vasoactive intestinal peptide (VIP). With the aim of investigating the possible cause-effect relationship between autoantibodies to VIP and asthma, the authors have cloned catalytic antibody light chains from the immune repertoire of a patient with exercise-induced. asthma. Here, the authors describe the application of phage- display techniques for the selection of antigen-specific light chains.

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=> S L1 AND (L9,L10,L11)
        175719 CATALYSIS
           419 CATALYSES
        175958 CATALYSIS
                  (CATALYSIS OR CATALYSES)
         33622 CATALYZES
        383617 CATALYTIC
            27 CATALYTICS
        383627 CATALYTIC
                  (CATALYTIC OR CATALYTICS)
        223017 CATALYZED
             1 CATALYZEDS
        223017 CATALYZED
                  (CATALYZED OR CATALYZEDS)
        431324 ANTIBOD?
          2269 (CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
           248 ABZYME
           155 ABZYMES
           295 ABZYME
                  (ABZYME OR ABZYMES)
L14           9 L1 AND ((L9 OR L10 OR L11))

=> S L14 NOT L2
L15           0 L14 NOT L2

=> S L14 NOT L12
L16           9 L14 NOT L12

=> D 1-9 CBIB ABS
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L16 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
2002:861199 Document No. 138:217276 A rat monoclonal antibody that catalyses the hydrolysis of a nitrophenyl-β-lactam. Ostler, Elizabeth L.; Dean, Christopher J.; Barber, Nicola; Valeri, Maurizio; James, Stuart; Resmini, Marina; Boucher, Guillaume; Romanov, Nickolas; Brocklehurst, Keith; Gallacher, Gerard (School of Pharmacy and Biomolecular Sciences, University of Brighton, Brighton, BN2 4GJ, UK). Biochemical and Biophysical Research Communications, 299(2), 273-276 (English) 2002. CODEN: BBRCA9. ISSN: 0006-291X. Publisher: Elsevier Science.

AB We report the first example of a monoclonal antibody- catalyzed hydrolysis of a β-lactam where the antibodies were generated by a simple transition-state analog. A rat monoclonal antibody (1/91c/4d/26) generated by using an acyclic 4-nitrophenylphosphate immunogen catalyzed the hydrolysis of corresponding 4-nitrophenyl carbonates but, more importantly, also catalyzed the hydrolysis of N-(4-nitrophenyl)-azetidinone at pH 8 with kcat=8.7 + 10-6 s-1 and Km=35 μM. This is the first example of a rat monoclonal catalytic antibody.

L16 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
2002:787386 Document No. 138:51714 Polyclonal catalytic antibodies. Ostler, Elizabeth L.; Resmini, Marina; Brocklehurst, Keith; Gallacher, Gerard (School of Pharmacy and Biomolecular Sciences, Division of Chemistry, University of Brighton, Brighton, BN2 4GJ, UK). Journal of Immunological Methods, 269(1-2), 111-124 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..

AB A review. Polyclonal catalytic antibodies offer advantages in the evaluation of immunogens and in the ease of production of large quantities of antibodies. They comprise the entire immune response of an animal to an immunogen where monoclonals represent a subset. Polyclonal antibodies are consequently particularly suitable for evaluating catalytic antibody responses generated by different haptens or a group of structurally related haptens. The authors reported the first polyclonal catalytic antibodies in 1990. An unexpected finding is that polyclonal catalytic antibodies show single-site kinetic behavior, i.e. whatever structural heterogeneity exists, the kinetic behavior is homogeneous. Many groups worldwide have since published work in this area. Three groups are prominent. The authors' group, a group based in Austin, Texas, and led by Iverson, and a Shanghai group. The authors' group works with sheep antibodies and has published mechanistic studies and more recently, specificity studies that revealed the catalysis of a β- lactam. Most of this work over a 10-yr period was performed by using a single bleed from a single sheep, which gives an indication of the ease of production and utility of such catalytic antibodies . Iverson's group works with rabbit antibodies and has published much work on the evaluation of catalytic antibodies generated by structurally related haptens. The Shanghai group has concentrated on the studies of polyclonal catalytic antibodies for electrocyclic reactions where any danger of contaminating enzymes is reduced. The use of immunization to generate therapeutically useful catalytic antibodies (necessarily polyclonal) in a host animal is an attractive target. Several groups are working towards this. The authors themselves have published in this area and promising recent studies come from a group working in France on immunization to protect against nerve agents and a Texas group (based in Houston) that has demonstrated active immunization to generate antibodies that catalyze the hydrolysis of a carbamate insecticide.

L16 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
2002:332361 Document No. 136:321704 Methods and compositions for modifying biologically active target molecules with catalytic antibodies. Martin, Mark T. (Igen International, Inc., USA). PCT Int. Appl. WO 2002034933 A2 20020502, 61 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US31663 20011010. PRIORITY: US 2000-PV242125 20001020.

AB The invention concerns a method of modifying a target substance by contacting the target substance with a catalyst that catalyzes the modification of the target substance. In a preferred embodiment, the method comprises labeling a target substance by contacting the target substance with a label and a catalyst that catalyzes the attachment of the label to the target substance. Preferably, the catalyst catalyzes selectively the reaction between a specific target mol. and a specific label. The attachment of labels may be used to inactivate a biol. active target substance or otherwise modulate its activity. Alternatively, the method may be used to label the target mol. with a detectable label suitable for the sensitive detection of the target substance.

L16 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2002:97746 Document No. 136:401553 Polyclonal antibody-catalyzed hydrolysis of a β-lactam. Ostler, Elizabeth L.; Resmini, Marina; Boucher, Guillaume; Romanov, Nickolas; Brocklehurst, Keith; Gallacher, Gerard (School of Pharmacy and Biomolecular Sciences, University of Brighton, Moulsecoomb, Brighton, BN2 4GJ, UK). Chemical Communications (Cambridge, United Kingdom) (3), 226-227 (English) 2002. CODEN: CHCOFS. ISSN: 1359-7345. OTHER SOURCES: CASREACT 136:401553. Publisher: Royal Society of Chemistry.

AB We report the first example of antibody-catalyzed hydrolysis of a β-lactam where the antibodies were generated by a simple transition-state analog; in this example the antibodies are polyclonal.

L16 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2001:150236 Document No. 134:322579 A suicide-substrate mechanism for hydrolysis of β-lactams by an anti-idiotypic catalytic antibody. Lefevre, S.; Debat, H.; Thomas, D.; Friboulet, A.; Avalle, B. (Genie Enzymatique et Cellulaire, UMR 6022 CNRS, Universite de Technologie de Compiegne, Compiegne, 60205, Fr.). FEBS Letters, 489(1), 25-28 (English) 2001. CODEN: FEBLAL. ISSN: 0014-5793. Publisher: Elsevier Science B.V..

AB The catalytic mechanism of an anti-idiotypic antibody, 9G4H9, displaying a β-lactamase activity was investigated. Kinetics expts. suggest that some penicillinic derivs. behave both as substrates and inactivators. Biochem. and immunol. expts. strongly indicate that ampicillin may be regarded as a suicide substrate for hydrolysis by 9G4H9. The anti-idiotypic network appears as a way to create enzyme mimics with modified catalytic activities.

L16 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2001:67204 Document No. 134:248789 Structure-function studies of a new generation of catalytic protein: an abzyme with a beta-lactamase activity. Debat, Helene; Avalle, Berangere; Friboulet, Alain; Thomas, Daniel (UPREs A 602 Genie Enzymatique et Cellulaire, Universite de Technologie de Compiegne, Compiegne, 60205, Fr.). International Journal of Bio-Chromatography, 5(2), 91-96, color plate p. 166 (English) 2000. CODEN: IJOBEQ. ISSN: 1068-0659. Publisher: Harwood Academic Publishers.

AB The previously described anti-idiotypic strategy for eliciting catalytic antibodies (abzymes) rests on the possibility to induce combining sites that mimic the structural features of enzymic active sites. A monoclonal anti-idiotypic IgG, 9G4H9, was previously obtained by using beta-lactamase as the

original antigen. This abzyme catalyzes the hydrolysis of opening of beta-lactam rings with a good efficiency. 9G4H9 variable regions were cloned and sequenced. While no significance homol. at primary structure level could be seen between the enzyme and the abzyme, the mol. modeling of 9G4H9 suggests that catalytic residues identical to that involved in the catalytic mechanism of the enzyme are present in 9G4H9.

L16 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
1998:524216 Document No. 129:227345 Functional mimicry: elicitation of a monoclonal antiidiotypic antibody hydrolyzing β-lactams. Avalle, Berangere; Thomas, Daniel; Friboulet, Alain (Laboratoire de Technologie Enzymatique-UPRES-A CNRS 6022, Universite de Technologie de Compiegne-BP 20529, Compiegne, 60205, Fr.). FASEB Journal, 12(11), 1055-1060 (English) 1998. CODEN: FAJOEC. ISSN: 0892-6638. Publisher: Federation of American Societies for Experimental Biology.
AB Antigen mimicry by anti-idiotypic antibodies is investigated as a reliable strategy to achieve mol. imprinting of an enzymic activity. A monoclonal anti-idiotypic antibody (Ab2-9G4H9) was elicited by using a monoclonal antibody (Ab1-7AF9) specific for the β-lactamase active site. Catalytic features of Ab2 were characterized with β-lactamase substrates. The antibody combining site appeared to have retained a part of the catalytic specificity. The relevance of the idiotypic mimicry concept for the generation of catalytic antibodies was further demonstrated by eliciting a third generation antibody (Ab3), which was shown to recognize β-lactamase: the complete internal image properties of Ab2 9G4H9, including binding and catalytic properties, were thus checked.

L16 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
1994:573768 Document No. 121:173768 An approach to sequence-specific antibody proteases. Smith, Robert, M.; Ping, Yuan; Weiner, David P.; Dutton, Caryn R.; Hansen, David E. (Dep. Chem., Amherst College, Amherst, MA, 01002, USA). Applied Biochemistry and Biotechnology, 47(2-3), 329-43 (English) 1994. CODEN: ABIBDL. ISSN: 0273-2289.
AB The authors describe here a novel strategy for the isolation of antibodies with sequence-specific protease activity: the synthesis of dipeptide haptens in which the targeted peptide bond has been replaced by a ring-strained or torsionally strained by hydroxyethylene transition-state analog. Thus, the analogs mimic both a peptide bond in a distorted, reactive conformation and the transition state for peptide bond hydrolysis. To obtain sequence-specific antibody proteases, these analogs have been flanked with addnl. amino acid residues in preparation for immunization. In particular, the authors have synthesized peptides containing analogs such as 2-cis-amino-3-cis-hydroxycyclobutane carboxylic acid and endo-(3-amino-2-hydroxy)bicyclo[2.2.1]-heptane-7-anti-carboxylic acid. The authors have also prepared a series of peptide derivs. containing analogs, such as 2-[3-amino-2-oxo-1-azetidinyl]-3-methylbutanoic acid, in which the targeted peptide bond has been incorporated into a β- lactam ring. Since the "peptide bond" has been left intact, these species mimic only a distorted ground state. At present, antibodies are being elicited against a number of the above peptide derivs.

L16 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
1993:54708 Document No. 118:54708 Catalytic antibodies: A new window on protein chemistry. Suckling, Colin J.; Tedford, Catriona M.; Proctor, George R.; Khalaf, Abedawn I.; Bence, Laura M.; Stimson, William H. (Dep. Pure Appl. Chem., Univ. Strathclyde, Glasgow, G1 1XL, UK). Ciba Foundation Symposium, 159(Catal. Antibodies), 201-10 (English) 1991. CODEN: CIBSB4. ISSN: 0300-5208.
AB A review with 10 refs. Catalytic antibodies have created a new dimension in protein chemical In these studies it is particularly valuable to investigate systems for which natural enzymic catalysts are unknown. Several ways of

preparing homochiral building blocks for organic synthesis have been examined by the authors. Antibodies that catalyze the Diels-Alder reaction have been characterized. The target reaction was the addition of acetoxybutadiene to N-substituted maleimides, a reaction that should give a pentafunctional homochiral building block. Catalytic antibodies can give insight into the mechanism of catalysis by proteins. An adventitious hydrolytic antibody that cleaves activated esters was investigated. An antibody raised to ampicillin for anal. purposes has also been shown to catalyze hydrolysis of the β-lactam ring.

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=> E MARTIN M/AU
=> S E3,E61-64,E241
           760 "MARTIN M"/AU
           107 "MARTIN M T"/AU
             1 "MARTIN M T CALVO"/AU
             1 "MARTIN M TEMPRANO"/AU
             8 "MARTIN M TERESA"/AU
             2 "MARTIN MARTIN"/AU
L17        878 ("MARTIN M"/AU OR "MARTIN M T"/AU OR "MARTIN M T CALVO"/AU OR
               "MARTIN M TEMPRANO"/AU OR "MARTIN M TERESA"/AU OR "MARTIN MARTIN
               "/AU)
=> S L17 AND L2
L18          0 L17 AND L2

=> S L17 AND (L3,L4,L5,L9,L10,L11)
L19          7 L17 AND ((L3 OR L4 OR L5 OR L9 OR L10 OR L11))

=> S L19 NOT (L12,L16)
L20          7 L19 NOT ((L12 OR L16))

=> D 1-7 CBIB ABS

L20  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2005 ACS on STN
2000:251470  Document No. 133:251104  Isolated hyperthermic liver perfusion
     with high dose tumor necrosis factor alpha in pigs: an experimental study
     in preparation of clinical use.  Lang, H.; Thyen, A.; Nadalin, S.;
     Frerker, M.; Moreno, L.; Flemming, P.; Martin, M.; Oldhafer, K.
     J.; Raab, R. (Klinik fur Abdominal-und Transplantationschirurgie,
     Medizinische Hochschule Hannover, Germany).  European Surgical Research,
     32(1), 1-10 (English) 2000.  CODEN: EUSRBM.  ISSN: 0014-312X.  Publisher:
     S. Karger AG.
AB   Isolated hyperthermic perfusion of the liver was performed for 45 min in 27 pigs
     via hepatic artery and portal vein at mean inflow temps. between 40.7 and 41.2°C.
     In two study groups B and C (n = 9 pigs each) 50 μg recombinant human tumor
     necrosis factor-α (rhTNFα) per kg body weight were added to the perfusate,
     whereas in a control group A liver perfusion was done without rhTNFα.  Before
     reperfusion the livers were washed out with Ringer's solution in all groups
     followed by a protein solution in group C.  At 30 and 60 min after reperfusion
     the maximum systemic rhTNFα concns. were significantly higher in group B with 68
     and 61 ng/mL compared to 14.5 and 14.9 ng/mL in group C.  Mean systemic porcine
     TNFα concentration was significantly higher in group B (217 pg/mL) compared to
     group C (50 pg/mL) 30 min after reperfusion.  Survival was 7/9 in group A and C
     and only 2/9 in group B with 6/7 pigs dying due to severe cardiopulmonary failure
     within 12 h after operation.  In surviving pigs of group A and C only mild and
     transient hepatotoxicity was registered.  The presented study underlines the
     feasibility of high dose rhTNFα application in an isolated hyperthermic liver
     perfusion system.  Washout of the liver with a protein solution before
     reperfusion reduces systemic TNFα levels as well as associated lethal
     cardiocirculatory and hepatotoxic side effects.

L20  ANSWER 2 OF 7  CAPLUS  COPYRIGHT 2005 ACS on STN
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1999:605484 Document No. 132:150437 Involvement of reactive oxygen species in TNF-α mediated activation of the transcription factor NF-κB in canine dermal fibroblasts. Kohler, H. B. K.; Knop, J.; Martin, M.; de Bruin, A.; Huchzermeyer, B.; Lehmann, H.; Kietzmann, M.; Meier, B.; Nolte, I. (Klinik fur kleine Haustiere, Tierarztliche Hochschule Hannover, Hannover, 30173, Germany). Veterinary Immunology and Immunopathology, 71(2), 125-142 (English) 1999. CODEN: VIIMDS. ISSN: 0165-2427. Publisher: Elsevier Science B.V..

AB The cytokine tumor necrosis factor-alpha (TNF-α) plays a major role in inflammatory and immune-pathol. reactions of the skin. With respect to a possible therapeutic modulation of TNF -α mediated activation of Nuclear Factor-kappa B (NF-κB) in canine cutaneous inflammation, we investigated the role of NF-κB and the involvement of reactive oxygen species (ROS) in the TNF-α signaling pathway in dermal fibroblasts of the dog. TNF-α treatment resulted in the activation of NF-κB as assessed by electrophoretic mobility shift assay (EMSA). Addnl., NF-κB translocation was induced with butylhydroperoxide and antimycin A, but not with hydrogen peroxide. TNF-α stimulated NF-κB activation was partially inhibited by preincubation with the antioxidants α-lipoic acid and butylated hydroxyanisol (BHA). No superoxide generation following TNF-α stimulation could be detected in the supernatant of canine fibroblasts with the superoxide dismutase-inhibitable cytochrome c reduction test. In contrast, production of TNF-α dependent intracellular hydrogen peroxide, the dismutation product of the superoxide radical, was demonstrated spectroscopically by formation of electron dense cerium-hydroperoxide ppts. With electron energy loss spectroscopy (EELS) significant cerium deposits were detected in the mitochondria, the endoplasmatic reticulum, the cytosol and to a lesser extent on the plasma membrane of canine fibroblasts indicating multiple hydrogen peroxide production sites. Peroxides, therefore, possibly play an important part in the redox-sensitive pathway of TNF-α dependent NF-κB activation in canine skin. An adjunctive therapy with appropriate antioxidants modulating NF-κB overactivation in cutaneous inflammation in the dog is promising.

L20 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

1999:574621 Document No. 131:283350 Histopathological and cellular studies of a case of cutaneous radiation syndrome after accidental chronic exposure to a cesium source. Vozenin-Brotons, M-C.; Gault, N.; Sivan, V.; Tricaud, Y.; Dubray, B.; Clough, K.; Cosset, J-M.; Lefaix, J-L.; Martin, M. (Laboratoire de Radiobiologie et Etude du Genome, DRR, DSV, CEA, Saclay, Fr.). Radiation Research, 152(3), 332-337 (English) 1999. CODEN: RAREAE. ISSN: 0033-7587. Publisher: Radiation Research Society.

AB This study was designed for the histopathol., cellular and biochem. characterization of a skin lesion removed surgically from a young male several months after accidental exposure to cesium-137, with an emphasis on expression of transforming growth factor β1 (TGFB1) and tumor necrosis factor α (TNFA) and the occurrence of apoptosis. Under a hypertrophic epidermis, a highly inhomogeneous inflammatory dermis was observed, together with fibroblastic proliferation in necrotic areas. Immunostaining revealed overexpression of TGFB1 and TNFA inside the keratinocytes of the hypertrophic epidermis as well as in the cytoplasm of the fibroblasts and connective tissue of the mixed fibrotic and necrotic dermis. Inside this dermis, the TUNEL assay revealed areas containing numerous apoptotic fibroblasts next to areas of normal viable cells. Overexpression of TGFB1 was found in the conditioned medium and cellular fractions of both hypertrophic keratinocytes and fibrotic fibroblasts. This overexpression lasted for at least three passages in tissue culture. The present observations were consistent with the central role of TGFB1 in the determination of chronic radiation-induced damage to the skin and a significant involvement of TNFA. In addition, programmed cell death appeared to take place during the remodeling of the mixed fibrotic and necrotic tissue.

L20 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

1999:492789 Document No. 132:34508 IFN-τ: a new type I IFN with antiretroviral activity. Clayette, P.; Martin, M.; Dereuddre-Bosquet, N.; Tournay, V.; Gras, G.; Martal, J.; Dormont, D. (CEA, Service de Neurovirologie, DSV/DRM, CRSSA, IPSC, Fontenay-Aux-Roses, 92265, Fr.). Pathologie Biologie, 47(5), 553-559 (French) 1999. CODEN: PTBIAN. ISSN: 0031-3009. Publisher: Expansion Scientifique Publications.

AB Type I interferon (IFN) such as IFN-α have demonstrated relative efficiency in HIV-infected patients with Kaposi's sarcoma. Nevertheless, their clin. uses have been restricted by several major side effects. IFN-τ is a non-cytotoxic type I IFN. In the present manuscript, we described its in vitro effects towards HIV replication and its mode of action. IFN-τ is a potent antiviral mol. that interferes with an early step of HIV biol. cycle. Moreover, it induces IL- 6 synthesis by macrophages, and this cytokine favors its antiviral efficacy, probably by amplifying the induction of 2', 5'-OAS and RNase L. Altogether, these results confirm the interest of IFN-τ as adjuvant therapy in HIV infection, and more particularly in HIV/HCV-infected patients.

L20 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

1997:402640 Document No. 127:134559 Experimental investigation of isolated liver perfusion with tumor necrosis factor α. Lang, Hauke; Nadalin, S.; Moreno, L.; Flemming, P.; Thyen, A.; Martin, M.; Oldhafer, K. J.; Pichlmayr, R. (Klinik Abdominal- Transplantationschirurgie, Medizinische Hochschule Hannover, Hannover, D-30625, Germany). Chirurgisches Forum fuer Experimentelle und Klinische Forschung 339-343 (German) 1997. CODEN: CFEKA7. ISSN: 0303-6227. Publisher: Springer.

AB Isolated hyperthermic liver perfusion was performed in swine (Group 1 and 2) via the hepatic artery and portal vein. Group 1 served as control group while in group 2 and 3 a total of 50 μg tumor necrosis factor α (TNF-α)/kg bw was administrated. Before reperfusion the livers were washed with Ringer's solution in group 1 and 2 and addnl. with a proteic-solution in group 3. Maximum TNF-. alpha.-concns. 1 h after reperfusion were 128 ng/mL (group 2) and 12 ng/mL (group 3). In group 2 all animals died within 12 h after reperfusion, while 5/7 swine TNF-α of group 3 survived. Functional and morphol. and morphol. studies did reveal irreversible hepatotoxic effects due to TNF-.alpha .33333. The study suggests the possibility of high dose TNF-. alpha. application in isolated hyperthermic liver perfusion.

L20 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

1997:354841 Document No. 127:75557 Pharmacodynamic effects of amoxicillin versus cefotaxime against penicillin-susceptible and penicillin-resistant pneumococcal strains: a phase I study. Aguilar, L.; Rosendo, J.; Balcabao, I. P.; Martin, M.; Gimenez, M. J.; Frias, J.; Prieto, J. (Medical Department, SmithKline Beecham Pharmaceuticals, Madrid, 28034, Spain). Antimicrobial Agents and Chemotherapy, 41(6), 1389-1391 (English) 1997. CODEN: AMACCQ. ISSN: 0066-4804. Publisher: American Society for Microbiology.

AB Serum bactericidal activity against a penicillin-susceptible strain and a penicillin-resistant strain of Streptococcus pneumoniae (amoxicillin and cefotaxime MICs, 0.001 and 1 μg/mL, resp., and MBCs, 0.01 and 2 μg/mL, resp.) was measured in 12 healthy volunteers who each received an oral 875-mg dose of amoxicillin and an i.m. 1-g dose of cefotaxime in a crossover fashion. The areas under the bactericidal activity-time curves for the two strains were found to be similar for both antibiotics despite the significantly higher ($P < 0.002$) AUC/MIC and peak level/MIC values for cefotaxime.

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1996:725642 Document No. 126:16675 Activities against Streptococcus

pneumoniae of amoxicillin and cefotaxime at physiological concentrations: in vitro pharmacodynamic simulation. Balcabao, I. P.; Aguilar, L.; Martin, M.; Garcia, Y.; Dal-Re, R.; Prieto, J. (Microbiol. Dep., Univ. Complutense, Madrid, 28034, Spain). Antimicrobial Agents and Chemotherapy, 40(12), 2904-2906 (English) 1996. CODEN: AMACCQ. ISSN: 0066-4804. Publisher: American Society for Microbiology.

AB An in vitro model simulating amoxicillin and cefotaxime concns. in human serum (after standard doses) was used to explore the activities of these drugs over time against penicillin-susceptible and penicillin-resistant Streptococcus pneumoniae strains. An initial inoculum reduction percentage of ≥90% was obtained with amoxicillin and maintained for 2 to 8 h, regardless of the strain tested. In contrast, expts. showed that cefotaxime had significantly ($P<0.001$) less capability to reduce initial inocula of the penicillin-resistant pneumococci from 0.5 h on than amoxicillin, despite the same in vitro susceptibility to amoxicillin and cefotaxime in both strains.